

Contact allergy from DMDM hydantoin, 1994–2000

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DMDM hydantoin (DMDMH, 1,3-dimethylol-5,5'-dimethylhydantoin, CAS 6440-58-0) is a preservative used mainly in cosmetics, with a MAC of 0.6% w/w, according to the EEC Cosmetic Directive 76/768/EEC

(1). Positive patch tests were first reported in 1982 from the US (2). De Groot et al. demonstrated cross-reactivity with formaldehyde (3) and substantiated clinical relevance by ROAT (4). It was therefore included in the topicals test panel of the German Contact Dermatitis Research Group (DKG) in 1994, with the results here presented and discussed.

Methods

In the centres of the IVDK listed above, simultaneously with members of the DKG, DMDMH was tested from the start of 1994 (2% aq.; Hermal, Reinbek, Germany). Results of the D3 readings following ICDRG guidelines, together with results of DMDMH 2% in pet. used initially by a few centres, and with formaldehyde (1% aq., in the standard series) are shown in Table 1. The statistical software package SAS 8.1 (SAS Institute, Cary, NC, USA) was used.

Results

Between January 1994 and December 2000, 67915 patients were patch tested, 62116 with formaldehyde, 1808 with DMDMH in pet. and 34321 with DMDMH in aq.

Analyses of cross-reactivity were based on the subset of patients tested for both DMDMH in aq. and formaldehyde. While reproducibility, i.e. the proportion of synchronously negative ($n = 32686$) and positive ($n = 67$) reactions, appears high (98.3%), concordance, as quantified by Cohen's kappa as a measure of chance corrected agreement, was quite limited (kappa: 0.18, 95% CI: 0.14–0.22). 488 patients were positive to formaldehyde, but not to DMDMH, with the opposite observed in 95 cases. From 1995 to 2000 (excluding 1994 because of DMDMH being introduced in the course of that year in several centres), the number of patients tested with DMDMH ranged between 5000 and 6000 per year. The proportion of positive reactions ranged between 0.39% and 0.65% in these years, with no evidence of a significant time trend (Cochrane-Armitage trend test, two-sided, $p = 0.22$).

In the majority of the 180 positive cases (Table 1), cosmetics (30%) or topical drugs (22%) were considered causal. Contact allergy to DMDMH was assessed as currently clinically relevant in 56 cases, 4 of these with occupational relevance, while previous clinical relevance was ascertained in 4 cases. In 91 cases no such relevance could be established, and in 35 cases no evaluation of clinical relevance was documented. Comparison of the demographic characteristics of patients with positive *versus* negative reactions to DMDMH reveals no conclusive pattern, except for age and possibly leg dermatitis (strongly associated with age) being associated with DMDMH positivity.

Discussion

Previous patch test studies with DMDM hydantoin (DMDMH) found sensitization frequencies between 3.4% (5) and 1.2% (3), most likely depending on the selectivity of patch testing, the amount of regionally or nationally typical exposure, and not least on the patch test preparation used, 1–2% DMDMH in pet. and 2 or 3% DMDMH in aq. having been used so far.

In our study, DMDMH was tested not in the standard series, i.e. in consecutive patients, but in the topicals test series, i.e. in aimed testing. Despite this, the frequency of sensitization found was comparatively low. However, exposure to DMDMH may still be relatively uncommon in (central) Europe. According to a chemical analysis of preservatives in moisturizers on the Swedish market, only 3 out of 100 products contained DMDMH (1). Similar data are not available for Germany or Austria, which hampers risk assessment.

Furthermore, cross-reactivity to formaldehyde, addressed meticulously by de Groot et al. (4), appears very limited in our population, compared to that study. Largely in accordance with one previous study which systematically evaluated occupational risk factors (5), we could find few cases with occupational relevance, within the limitations of this kind of study. In conclusion, DMDMH seems to warrant further

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Table 1. Patch test results, 1994–2000 (readings at D3)

Allergen	<i>n</i> _(test)	Reaction				% positive
		?	IR	+	++/+++	
DMDM hydantoin, 2% pet.*	1808	14	2	5	1	0.3
DMDM hydantoin, 2% aq.*	34321	188	34	152	22	0.5
Tested in 35083 of these patients:						
Formaldehyde, 1% aq.	35083	419	71	456	147	1.6

*Duplicate testing in 8 patients, none reacting positively.

monitoring, especially in the possible event of increased future use.

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